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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/249,220	02/12/1999	RICHARD A. MUELLER	SRL-6109	9695

7590 12/23/2003

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/249,220	MUELLER ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-150* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-11,15-19,23-27,31-35,39-43,47-52,56-63 and 67-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4-6,12-14,20-22,28-30,36-38,43-45,52-54,63-65,72-74 and 78-150.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-76 in the paper filed August 25, 2003 (which applicant apparently faxed in on August 7, 2003), is acknowledged. Applicant's further election of the species N-(n-nonyl)-1,5 –dideoxy – 1, 5, imino-D-glucitol filed October 29, 2003, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 4-6, 12-14, 20-22, 28-30, 36-38, 43-45, 52-54, 63-65, 72-74 and 78-150 are drawn to non elected Groups and are withdrawn from further consideration.

Claim Objections

3. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 42-149 been renumbered 43-150. Specifically, there are two claims numbered "claim 42". Therefore, the second claim numbered 42 is newly numbered 43, and the remaining claims are renumbered as per this error.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

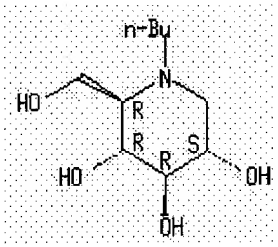
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-3, 7-11, 15-19, 23-27, 31-35, 39-40, 59-63, 67-77, 76 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Block et al (WO 95/19172) in view of Partis et al (U.S. Patent 5,303,638).

Block teaches a method for treating a hepatitis virus infection in a mammal (see abstract) comprising:

(a) administering to said mammal an anti-hepatitis virus effective amount of at least one N-substituted-1,5, dideoxy 1,5-imino-D-glucitol compound (see page 17 and page 18, claim 1) of the formula below:



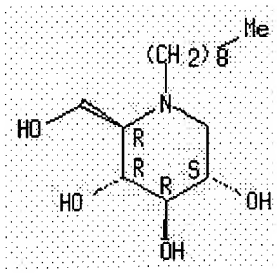
where R is a straight chain alkyl with four carbons and where W, X, Y and Z are hydrogen (see page 4 and page 18, claim 2).

With regard to claims 8, 16, 24, 32, 40, 61, 68, 70, and 77, Block teaches the pharmaceutically acceptable salt, HCL with the DNJ compound (see page 17, paragraph 2).

With regard to claim 59, Block teaches the use of between 1 and 1000 milligrams of compound for daily dosage, which falls within and significantly overlaps the range of 0.5 mg to 500 milligram per person of claim 59 (see page 17, paragraph 4).

While Block expressly suggests that the size of the alkyl group can be modified, and teaches a range of 3 to 6 carbon atoms (see page 4, line 5), Block does not expressly teach the use of 9 carbon atoms as in the nonyl DNJ molecule elected.

Partis teaches the use of nonyl DNJ of the formula below, which is identical to the elected species, for treatment of viruses and motivates their use (see column 3, lines 31-55, for example).



Where R is a straight chain alkyl with nine carbons and where W, X, Y and Z are hydrogen (see columns 3 and 4).

With regard to claims 2, 3, 7, 9-11, 15, 17-19, 23, 25-27, 31, 33-35, 39, 60, 62, 63, 68, 69, 71, 72, 76, Partis teaches the nonyl DNJ (see column 3, lines 31-55).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the 3 to 6 carbon chain length of the alkyl DNJ compound used to treat hepatitis virus of Block by increasing the number of carbons in the chain to 9 since Partis teaches that the pharmacokinetics of nonyl-DNJ were superior to butyl DNJ. Partis specifically states,

> "In preliminary pharmacokinetic tests, the illustrative N-nonyl-DNJ surprisingly exhibited a half-life of 5 times that of the N-butyl-DNJ when administered in vivo in rats. That is, the N-nonyl-DNJ has a t1/2 in vivo in the rat of 6.24 hours when measured as total radioactivity in the blood compared to the t1/2 of N-butyl-DNJ which is only 1.24 hours. The longer half-life allows less frequent dosing of the mammal to maintain effective blood concentrations of the antiviral agent and prevents wide variations in blood levels. Less frequent drug administration should also reduce the gastrointestinal side effects seen with N-butyl-DNJ. Although the inventors are not to be bound by theory, it is believed that the increase in half-life may be partially due to increased lipophilicity and to increased chain length. Increased lipophilicity should allow increased penetration of the cell membrane and thus provide a higher intercellular concentration relative to surrounding

body fluids."

Thus, an ordinary practitioner would have been motivated to use the nonyl DNJ of Partis in the place of the butyl DNJ of Block since Partis demonstrates that the nonyl DNJ has a longer half life, which permits less frequent dosing, which should reduce gastrointestinal side effects and should be longer acting. Further, Partis notes that this will result in a higher intracellular concentration (see column 3, lines 30-50). Further, Partis notes that the higher chain alkyls have increased potency against the target enzyme and reduced IC-50 values, making them more active and effective (see column 3, lines 20-31). Further, MPEP 2144.09 notes "Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties." In this case, the broadest generic claim differs from Block only in the addition of a single CH2 group that is successively added to an alkyl chain. Partis teaches the desirability of such an addition and motivates the nonyl DNJ which is the elected species.

7. Claims 41-43, 47-52, and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Block et al (WO 95/19172) in view of Partis et al (U.S. Patent 5,303,638) as applied claims 1-3, 7-11, 15-19, 23-27, 31-35, 39-40, 59-63, 67-77, 76 and 77 and further in view of Schinazi et al (U.S. Patent 5,444,063).

Block in view of Partis teach the limitations of claims 1-3, 7-11, 15-19, 23-27, 31-35, 39-40, 59-63, 67-77, 76 and 77 as discussed above. Further, Block teaches "Effective antiviral therapy for HBV (Hepatitis B virus) is likely to involve multiple strategies, including agents that influence the host immune system as well as those that interfere with different steps in the life cycle of the virus (see page 2, paragraph 2)." This is a direct suggestion to combine therapies.

Schinazi teaches combination therapy for hepatitis B virus using 3TC (see column 4, lines 36-54).

With regard to claims 50-52, and 55-57, Schinazi further teaches dosing of the 3TC between 0.1 to 100 mg per kg per day (see column 11, line 60-67 and column 12).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the therapy of Block in view of Partis with the therapy of Schinazi since Bock expressly teaches the concept of combination therapy with the DNJ compounds, stating "Effective antiviral therapy for HBV is likely to involve multiple strategies, including agents that influence the host immune system as well as those that interfere with different steps in the life cycle of the virus (see page 2, paragraph 3)." Further motivation is provided by Schinazi, who states "In one embodiment of the invention, one or more of the active compounds is administered in an alternative fashion with one or more other anti-HBV agents, to provide effective anti-HBV treatment. Examples of anti-HBV agents that can be used in alternation therapy include but are not limited to the (-)-enantiomer or racemic mixture of 2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane ("FTC", see

WO92/14743), its physiologically acceptable derivative, or physiologically acceptable salt; (-)-enantiomer or racemic mixture of 2-hydroxymethyl-5-(cytosin-1-yl)-1,3-oxathiolane (also referred to as "BCH-189" or 3TC) (see column 4, lines 36-54)."

Thus, an ordinary practitioner would have been faced by two references, each teaching compounds for antiviral therapy for HBV, Block using a DNJ compound and Schinazi using 3TC, each reference teaching that combination of the compound with other antiviral agents will improve efficacy. An ordinary practitioner would therefore have been motivated to combine the two prior art antiviral agents for the reason given in the prior art, to improve efficacy of treatment.

Double Patenting

8. The most recent claim set of copending application 09/355,446 was unavailable. Therefore, this rejection is made using the older claim set.

9. Claims 1-3,7-11,15-19,23-27,31-35,39-43,47-52,56-63 and 67-77 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of copending Application No. 09/355,446. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are drawn to both monotherapy with nonyl DNJ and combination therapy with DNJ. The claims of copending application 09/355,446 are drawn to combination therapy. Thus, the copending claims represent a species of the broader current claims and the species anticipates, and necessarily renders obvious, the more generic claims to treatment "comprising" or "consisting essentially of" nonyl DNJ.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Response to Arguments

11. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is currently 703-308-6568. In mid January, 2004, when TC 1600 relocates to the new USPTO facility in Alexandria, the examiner's phone number will become 571-272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The supervisor's new

telephone number in mid January will be 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is currently 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634